Comparison of Epigenetic Mediator Expression and Function in Mouse and Human Embryonic Blastomeres.

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Authors: Shawn L Chavez, Sohyun L McElroy, Nancy L Bossert, Christopher J De Jonge, Maria Vera Rodriguez, Denise E Leong, Barry Behr, Lynn M Westphal, Renee A Reijo Pera

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Public Summary:
A map of human embryo development that combines imaging, molecular, genetic and epigenetic data for comparisons to other species and across pathologies would be greatly beneficial for basic science and clinical applications. Here, we compared mRNA and protein expression of key mediators of DNA methylation and histone modifications between mouse and human embryos, embryos from fertile/infertile couples, and following growth factor supplementation. We observed that individual mouse and human embryos are characterized by similarities and distinct differences in DNA methylation and histone modification patterns especially at the single cell level. In particular, while mouse embryos first exhibited sub-compartmentalization of different histone modifications between blastomeres at the morula stage and cell sub-populations in blastocysts, differential histone modification expression was detected between blastomeres earlier in human embryos at the 4- to 8-cell stage. Likewise, differences in epigenetic mediator expression were also observed between embryos from fertile and infertile couples, which were largely equalized in response to growth factor supplementation, suggesting that select growth factors might prevent alterations in epigenetic profiles during prolonged embryo culture. Finally, we determined that reduced expression via morpholino technologies of a single histone-modifying enzyme, Rps6ka4/Msk2, resulted in cleavage-stage arrest as assessed by time-lapse imaging and was associated with aneuploidy generation. Taken together, data document differences in epigenetic patterns between species with implications for fertility and suggest functional roles for individual epigenetic factors during pre-implantation development.

Scientific Abstract:
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